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Effects of Indoor and Ambient Black Carbon and $PM_{2.5}$ on Pulmonary Function among Individuals with COPD

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Background: Particulate matter (PM) air pollution has been associated with decreased pulmonary function, but the exposure–response relationship in chronic obstructive pulmonary disease (COPD) patients is uncertain, and most studies have only focused on exposures to ambient pollution.

Objectives: We aimed to assess associations between pulmonary function and indoor and ambient PM $\leq$ 2.5 μm ($PM_{2.5}$) and black carbon (BC).

Methods: Between November 2012 and December 2014, 125 patients with COPD (mean age, 73.4 y) who were not currently smoking and without known indoor BC sources were recruited. Indoor BC and $PM_{2.5}$ were measured in each home for a week in each season, up to four times a year, followed by in-person spirometry pre- and post-bronchodilator. Ambient exposures were available from a central site monitor. Multivariable adjusted mixed effects regression models were used to assess associations scaled per interquartile range (IQR) of exposure.

Results: There were 367 study visits; the median (IQR) indoor BC and $PM_{2.5}$ were 0.19 (0.22) $\mu g/m^3$ and 6.67 (5.80) $\mu g/m^3$, respectively. Increasing indoor exposures to BC were associated with decreases in pre-bronchodilator forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC), and FEV_1/FVC. For example, in multivariable adjusted models, each IQR increase in indoor BC from the weekly integrated filter was associated with a 17.87 mL [95% confidence interval (CI): −33.76, −1.98] decrease in pre-bronchodilator FEV_1. Increases in indoor $PM_{2.5}$ were associated with decreases in FEV_1 and FVC of smaller magnitude than those for indoor BC; however, the results were less precise. Ambient BC was not associated with pre-bronchodilator pulmonary function, ambient $PM_{2.5}$ was only associated with decreases in FVC and increases in FEV_1/FVC, and neither indoor nor ambient BC or $PM_{2.5}$ were associated with post-bronchodilator pulmonary function.

Conclusions: Low-level exposures to indoor BC and $PM_{2.5}$, but not ambient exposures, were consistently associated with decreases in pre-bronchodilator pulmonary function. There was no association between exposures and post-bronchodilator pulmonary function. https://doi.org/10.1289/EHP3668

Introduction

Chronic obstructive pulmonary disease (COPD) is a common disease that results in considerable morbidity and mortality. According to the most recent Global Burden of Disease estimates, 174.5 million individuals worldwide have COPD, and 3.2 million deaths from COPD occurred in 2015 (Soriano et al. 2017). Recent reviews and meta-analyses have summarized the current literature and suggest that particulate matter ≤2.5 μm ($PM_{2.5}$) exposure is a risk factor for incidence of COPD and that short-term exposures have been associated with increased rates of hospitalization, increased mortality, and an increased risk of exacerbations (Li et al. 2016; Sint et al. 2008). Several of these studies have suggested that $PM_{2.5}$ originating from traffic may be associated with larger effects (Bell et al. 2009; Gan et al. 2013; Peng et al. 2009; Zanobetti and Schwartz 2006).

Exposures to $PM_{2.5}$ have also been consistently associated with decreases in pulmonary function in general population epidemiologic studies (Chen et al. 2017; Huang et al. 2016; Lepeule et al. 2014; Rice et al. 2013; Santos et al. 2016; Thaller et al. 2008; Ulvestad et al. 2015; Wu et al. 2014; Zhao et al. 2015; Zuurbier et al. 2011). However, most of these studies have examined the impacts of ambient, not indoor, short-term exposures, and few studies have been conducted in populations of individuals with COPD. In a recent meta-analysis of studies among individuals with COPD, outdoor exposures to PM $\leq$ 10 μm (PM_{10}) were associated with a small decrease in forced expiratory volume in 1 s [(FEV_1) (−3.38 mL; 95% confidence interval (CI): −6.39, −0.37 per 10 $\mu g/m^3$] (Bloemsma et al. 2016). This has been supported by a recent study of outdoor exposures in London that enrolled both individuals with COPD and healthy volunteers (Sinharay et al. 2018). However, since patients with COPD typically spend most of their time indoors, the impact of indoor exposures may be especially important. Therefore, in this study, our objective was to assess the impacts of indoor exposures to $PM_{2.5}$ and black carbon (BC), primarily infiltrating from outdoor sources, on pulmonary function in a longitudinal panel study of COPD patients. We also wanted to compare the impacts of indoor exposures to those from ambient levels measured at a central monitoring location.

Methods

Study Population

The COPD and Air Pollution Study enrolled individuals with COPD between November 2012 and December 2014 from Eastern Massachusetts. Potential participants were identified through

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reviews of encounters with an ICD-9 code of 490-493 or 496 in the VA Boston pulmonary and primary care clinic and pulmonary function laboratory encounters. Potential participants were sent a study invitation letter with telephone follow-up. Participants were also recruited through flyers placed at VA Boston locations. Individuals were eligible for the study if they were 40 y of age or older, had an FEV_1/forced vital capacity (FVC) <0.70 on post-bronchodilator spirometry, or in their medical records had emphysema reported based on a clinical CT scan. Since COPD may occur in the absence of a smoking history or in individuals with chronic asthma (Lamprecht et al. 2011; Salvi and Barnes 2009), individuals were eligible regardless of smoking history or if under care for chronic asthma. We excluded any individuals with a history of malignancies other than local skin or stable prostate cancer, with any systemic inflammatory disease (e.g., rheumatoid arthritis), who were current smokers or lived with a current smoker, or who had a major known source of indoor air pollution (e.g., wood stove or fireplace, burning of incense or candles). Inclusion and exclusion criteria were confirmed at an initial screening visit. Eligible participants were asked to return for four additional clinic visits, spaced approximately 3 months apart. All visits were scheduled with the participant in stable clinical status (a minimum of 2 weeks after completion of antibiotics or steroids for a COPD exacerbation). The study protocol was approved by the Institutional Review Boards of VA Boston Healthcare System and Harvard Medical School, and participants provided informed consent.

Pulmonary Function Measures

Spirometry (HDpft 1000; Nspire) pre- and post-180 μg of albuterol (2 puffs) administered by a valved spacer was conducted using American Thoracic Society methods (Miller et al. 2005). The highest values of pre- and post-bronchodilator FEV_1 and FVC from acceptable efforts were used. Usual bronchodilator medications were not withheld before testing.

Exposure Assessment

For the week prior to each visit, subjects were asked to place a small particle sampler in their home to collect $PM_{2.5}$ on Teflon filters, which were subsequently analyzed for BC as a measure of traffic-related particles and $PM_{2.5}$ as a measure of more general particles. Samplers were shipped to eligible participants or given to them at the initial screening visit and were returned by express shipping or in person at the study visit. Participants were instructed to run the sampler for the week before their visit and to place the sampler in the room where they spent most time, excluding the kitchen. Sampler pumps (VP0140; Medo USA) were preset to a flow rate of 1.8 L/min and used a Harvard Personal Exposure Monitor with a size-selective impactor to collect particles with a 2.5 μm cutoff (Demokritou et al. 2001). Teflon filters were equilibrated in a temperature- and humidity-controlled room and weighed using a Mettler MT5 electronic microbalance before they were provided to participants and after they were returned. BC was measured using an EEL M43D Smokestain Reflectometer (Diffusion Systems) that determines the blackness of PM filter samples. Each filter served as its own blank (measured before and after sampling), yielding the net micrograms of BC in $PM_{2.5}$ mass. $PM_{2.5}$ and BC concentrations were calculated by dividing the net micrograms by the total volume of air sampled.

The integrated filter measures of BC and $PM_{2.5}$ reflect average exposures during each 1-wk sampling period. However, we were also interested in estimating the impact of daily exposures within each sampling week and therefore used information from a central site monitor to obtain estimates of daily exposure on the day of spirometry and the preceding 3 days. Daily measures of outdoor BC and $PM_{2.5}$ were available from the monitor located on top of the Countway Medical Library in Boston, Massachusetts (Kang et al. 2010). The daily values from the central site were used as weights to estimate daily values for each home as follows: $Indoor\ daily = \frac{Outdoor\ measured\ daily}{Outdoor\ measured\ weekly} \times Indoor\ measured\ weekly$. Daily estimates were calculated for each participant only for the days he/she ran the sampler. Previously, we found that BC at this central site captures temporal variability of BC at sites throughout Eastern Massachusetts (Gryparis et al. 2007; Tang et al. 2018). We also demonstrated that the infiltration rate of fine particles from outdoors to indoors varies little over 7 d (Brown et al. 2009). Therefore, given the absence of significant indoor sources, indoor levels are assumed to be proportional to outdoor levels and reflect infiltration of outdoor pollution.

Potential Confounders

Potential confounders were selected *a priori* based on their known associations with the outcomes or exposures. Self-reported race [white (regardless of ethnicity) vs. other (American Indian/Alaskan Native, Asian, Native Hawaiian or Other Pacific Islander, Black or African American, or Other)], gender (male/female), educational attainment (less than high school, high school, greater than high school), and marital (single, married, widowed/separate/divorced), and employment status (retired, currently working, not currently working) were collected at the first clinic visit. Date of birth was also collected and was used to calculate age at each clinic visit. Height and weight were measured at each visit and used to calculate body mass index (BMI). Pulmonary medication use (inhaled steroids, long-acting bronchodilators, and short-acting bronchodilators) was updated at each visit. At each visit, each participant was also asked if he/she felt as if he/she had experienced a cold, influenza, or other respiratory illness in the past 2 weeks.

The home addresses of each participant were geocoded using ArcGIS (version 10.4; ESRI) to obtain latitude and longitude. Daily outdoor temperature (at a 1×1 km scale) for each residence was estimated using a validated model that used a combination of satellite remote sensing of surface temperature, land use (e.g., greenness), and data from ground-level weather stations measuring air temperature to derive predictions for each address. In a cross-validation on left-out weather stations, the model had an R^2 of 0.95 (Kloog et al. 2014). Daily relative humidity information was available from the Boston Logan International Airport. Additional seasonal factors were controlled by categorizing the month of the clinical visit into one of four categories [winter (December, January, February), spring (March, April, May), summer (June, July, August), or fall (September, October, November)].

Statistical Analyses

Associations between an interquartile range (IQR) increase in BC or $PM_{2.5}$ and each pulmonary function measure were estimated using repeated measures regression with a random intercept for each participant (PROC MIXED; SAS 9.4; SAS Institute, Inc.). Deviations from linearity for each exposure response function were assessed using splines (R mgcv package; version 3.1.2; R Development Core Team) (Wood et al. 2016; Wood 2017). To estimate the statistical significance ($p < 0.05$) of any potential deviations from linearity, we conducted likelihood ratio tests comparing the model with a linear term to a model with the spline term. Exposures included average indoor BC and $PM_{2.5}$ concentrations from the integrated filter, average and daily ambient concentrations (measured at the central site) for the same

days as the indoor samples, and estimated indoor concentrations on the day of spirometry (lag0) and the 3 days before testing (individual lag days 1–3). Each exposure was examined in a separate model to obtain beta estimates and 95% CIs for each pulmonary function measure, and an alpha level of 0.05 was used to determine statistical significance. Participants without available exposure data for a given exposure were excluded from analyses of that exposure. For example, all participants who unplugged their sampler the night before the clinic visit were not included in the models of lag0 exposures. All models were adjusted for current age (continuous), gender (male/female), race (white/other), season (indicator terms for spring, summer, winter, and fall), and height (continuous, for models including FEV_1 and FVC). Additional potential confounders {BMI (continuous), medication use (indicator variables for long-acting bronchodilators, short-acting bronchodilators, and inhaled steroids), self-reported respiratory illness in past 2 wk (yes/no), socioeconomic status [educational attainment (indicator variables for less than high school, high school, or greater than high school)], marital status (never married/widowed or divorced/married), employment status (retired/currently working/currently not working), and outdoor ambient temperature (continuous) and relative humidity (continuous)} on the day of spirometry were separately included in models adjusted for age, gender, race, and season to assess if they changed the main effect estimates. All considered potential confounders were included in the final multivariable models.

Results

Characteristics of the 125 study participants and 367 clinic visits are presented in Table 1. The participants had an average age of 73.4 ± 8.6 y, were mostly white males, had an average BMI of $30.2 \pm 5.8\ kg/m^2$, had a high school education or greater, and only six (4.8%) were never smokers. Approximately a quarter of participants had been diagnosed with diabetes, and most were taking at least one pulmonary medication. The average pre-bronchodilator FEV_1, FVC, and FEV_1/FVC were 1.82 ± 0.60 L, 3.32 ± 0.80 L, and 0.55 ± 0.13, respectively. The equivalent post-bronchodilator values were 1.93 ± 0.16 L, 3.46 ± 0.81 L, and 0.56 ± 0.13. The sampler ran indoors for a mean of 7.6 days (range 4–10). The distributions of all exposure measures and the indoor/outdoor ratio for the integrated filter are presented in Table 2. The average indoor measured $PM_{2.5}$ on the integrated filter was $8.61 \pm 6.34\ \mu g/m^3$ [median (IQR) = 6.67 (5.80)], and the average indoor measured BC on the integrated filter was $0.24 \pm 0.28\ \mu g/m^3$[(median (IQR) = 0.19 (0.22)] (Table 2). The average indoor/outdoor ratio for $PM_{2.5}$ was 1.48 ± 1.20, and the average indoor/outdoor ratio for BC was 0.46 ± 0.67. Histograms of the integrated filter measures and the indoor/outdoor exposure ratios are shown in Figure S1.

Effect estimates for models adjusted for age, race, gender, and season with and without additional adjustment for other potential confounders are shown in Table S1. We present the associations for the fully adjusted models in all subsequent figures. There were no statistically significant deviations ($p > 0.05$) from linearity observed (data not shown); therefore, we present effect estimates from linear models. The multivariable adjusted associations between each measure of indoor or ambient exposure and pre-bronchodilator FEV_1 are presented in Figure 1. Increases in indoor $PM_{2.5}$ were associated with decreases in FEV_1. For example, each IQR increase in measured indoor $PM_{2.5}$ from the integrated filter ($5.80\ \mu g/m^3$) was associated with a 4.64 (95% CI: −23.39, 14.11) mL decrease in FEV_1. Associations with ambient $PM_{2.5}$ were less consistent; the effect estimates for lag0 and lag1 were negative, while the effect estimates for lag2, lag3, and ambient averages for the full sampling period were positive. Increases in indoor BC were associated with decreases in FEV_1 for all examined time

Table 1. Characteristics of study participants at baseline ($n = 125$) and outcomes, exposures, medication use, and other characteristics at each clinic visit (≤4 for each participant, $n = 367$) among chronic obstructive pulmonary disease (COPD) patients living in Eastern Massachusetts, United States (2012–2014).

	Mean ± SD or *n* (%)	Median (IQR)
Baseline characteristics of the 125 participants	—	—
Age (y)	73.1 ± 8.6	72.8 (12.8)
BMI (kg/m^2)	30.2 ± 5.8	29.8 (8.0)
Race	—	—
White	115 (92.0)	—
Other	10 (8.0)	—
Sex	—	—
Male	122 (97.6)	—
Female	3 (2.4)	—
Marital status	—	—
Never married	17 (13.6)	—
Widowed/divorced	54 (43.2)	—
Married	54 (43.2)	—
Educational attainment	—	—
Less than high school	19 (15.2)	—
High school	40 (32.0)	—
Greater than high school	66 (52.8)	—
Employment status	—	—
Retired	89 (71.2)	—
Currently working	20 (16.0)	—
Currently not working	16 (12.8)	—
Smoking status	—	—
Former	119 (95.2)	—
Never	6 (4.8)	—
Pack-years (ever smokers only, $n = 119$)	60.5 ± 39.2	52.0 (39.5)
Self-reported comorbidities	—	—
Heart Disease	65 (52.0)	—
Hypertension	24 (19.2)	—
Diabetes	31 (24.8)	—
Characteristics from the 367 visits	—	—
Pre-bronchodilator[a]	—	—
FEV1 (L)	1.82 ± 0.60	1.78 (0.85)
FVC (L)	3.32 ± 0.80	3.26 (0.98)
FEV_1/FVC	0.55 ± 0.13	0.57 (0.17)
Post-bronchodilator[b]	—	—
FEV1 (L)	1.93 ± 0.61	1.92 (0.91)
FVC (L)	3.46 ± 0.81	3.38 (1.00)
FEV_1/FVC	0.56 ± 0.13	0.58 (0.17)
Ambient residential temperature (°C)[c]	10.5 ± 9.6	11.6 (15.4)
Ambient relative humidity (%)[d]	65.7 ± 16.3	67.0 (26.6)
Days of indoor home sampling (*n*)	7.6 ± 0.7	8.0 (1.0)
Time indoors at home on weekdays (h)	17.1 ± 3.9	18.0 (6.0)
Time indoors at home on weekends (h)	17.1 ± 4.7	18.0 (7.0)
Distance to central site monitor (km)	27.1 ± 20.3	23.1 (28.1)
Season	—	—
Winter	78 (21.3)	—
Spring	91 (24.8)	—
Summer	95 (25.9)	—
Fall	103 (28.1)	—
Pulmonary medication use	—	—
Inhaled steroids[e]	276 (75.2)	—
Long-acting bronchodilators[e]	—	—
Long-acting muscarinic antagonists	239 (65.1)	—
Long-acting β2 agonists	237 (65.4)	—
Theophylline	4 (1.1)	—
Short-acting bronchodilators[f]	279 (76.0)	—
Cold or other respiratory illness in 2 wk before testing	53 (14.4)	—

Note: —, no data; BMI, body mass index; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; IQR, interquartile range; SD, standard deviation.
[a]Spirometry performed prior to the administration of albuterol (2 puffs).
[b]Spirometry performed after the administration of albuterol (2 puffs).
[c]Average temperature on the day of spirometry estimated at the residential address predicted using the spatiotemporal model described in Kloog et al. 2014.
[d]Average relative humidity on the day of spirometry measured at Boston Logan International Airport.
[e]Self-report of a current prescription.
[f]Self-report of use within 6 h of pre-bronchodilator spirometry.

Table 2. Distributions of indoor and ambient particulate matter ≤2.5 μm ($PM_{2.5}$) and black carbon (BC) exposures, and the ratio of indoor to central site ambient exposures from 367 sampling sessions from 125 chronic obstructive pulmonary disease (COPD) patients living in Eastern Massachusetts, USA (2012–2014).

	n	n Miss[b]	Mean ± SD	Median	IQR[a]
Indoor exposure	—	—	—	—	—
$PM_{2.5}$ ($\mu g/m^3$)	—	—	—	—	—
Integrated filter	367	0	8.61 ± 6.34	6.67	5.80
Individual lags[c]	—	—	—	—	—
0	273	94	8.69 ± 8.66	6.14	6.13
1	330	37	8.42 ± 7.67	6.13	5.83
2	340	27	8.61 ± 8.14	6.43	6.01
3	344	23	8.72 ± 7.65	6.43	6.86
BC ($\mu g/m^3$)	—	—	—	—	—
Integrated filter	367	0	0.24 ± 0.28	0.19	0.22
Individual lags[c]	—	—	—	—	—
0	271	96	0.26 ± 0.36	0.18	0.25
1	329	38	0.23 ± 0.29	0.17	0.24
2	336	31	0.23 ± 0.31	0.16	0.24
3	339	28	0.22 ± 0.28	0.16	0.20
Ambient exposure	—	—	—	—	—
$PM_{2.5}$ ($\mu g/m^3$)	—	—	—	—	—
Individual Lags[c]	—	—	—	—	—
0	273	94	6.41 ± 3.62	5.21	3.74
1	330	37	6.13 ± 3.53	5.09	3.80
2	340	27	6.25 ± 3.43	5.31	3.95
3	344	23	6.32 ± 3.50	5.32	4.16
BC ($\mu g/m^3$)	—	—	—	—	—
Individual lags[c]	—	—	—	—	—
0	271	96	0.64 ± 0.40	0.54	0.42
1	329	38	0.57 ± 0.37	0.47	0.39
2	336	31	0.53 ± 0.33	0.44	0.39
3	339	28	0.53 ± 0.33	0.42	0.38
$PM_{2.5}$ Indoor/central site ratio	367	0	1.48 ± 1.20	1.10	0.94
BC indoor/central site ratio	367	0	0.46 ± 0.67	0.35	0.41

Note: —, no data; SD, standard deviation.
[a]IQR = interquartile range (75th to 25th percentile).
[b]Participants are missing individual lags for any day the in-home sampler was not measuring exposures.
[c]Lag numbers indicate days prior to spirometry (e.g., lag0 is the day of testing).

windows. For example, each IQR increase in measured indoor BC from the integrated filter (0.22 $\mu g/m^3$) was associated with a 17.87 (95% CI: −33.76, −1.98) mL decrease in FEV_1, with similar effect estimates for each of the individual lag days (lag0–3). Associations with ambient BC were less consistent, with both positive and negative effect estimates.

The associations with pre-bronchodilator FVC are presented in Figure 2. Increases in both indoor and ambient $PM_{2.5}$ were associated with decreases in FVC, with effect estimates ranging from −5.85 (95% CI: −35.02, 23.33) mL for an IQR increase (3.80 $\mu g/m^3$) in lag1 ambient $PM_{2.5}$ to −21.28 (95% CI: −43.99, 1.43) mL for an IQR increase in lag0 (6.13 $\mu g/m^3$) indoor $PM_{2.5}$. There was less evidence of an association between indoor or ambient BC with FVC, with both positive and negative associations observed, although the majority of indoor BC associations were negative.

Associations with pre-bronchodilator FEV_1/FVC are presented in Figure 3. IQR increases in both indoor and ambient $PM_{2.5}$ were positively associated with FEV_1/FVC, though effect estimates were generally close to the null with wide CIs. IQR increases in indoor BC were associated with lower FEV_1/FVC for all time periods, while all estimates for ambient BC were close to the null.

Patterns of associations for indoor and ambient $PM_{2.5}$ and BC with post-bronchodilator FEV_1, FVC, and FEV_1/FVC were generally consistent with associations for pre-bronchodilator measures, though negative associations with indoor BC tended to be weaker for all three outcomes, and associations between indoor $PM_{2.5}$ and post-bronchodilator FEV_1/FVC were null or slightly negative instead of slightly positive (Figures S2–S4).

Discussion

In this study of 125 patients with COPD examined up to four times, we observed that increasing indoor exposures to BC, a marker of traffic exposure, were associated with lower pre-bronchodilator FEV_1, FVC, and FEV_1/FVC, while indoor $PM_{2.5}$ was associated with smaller decreases in FEV_1 and FVC. Although small, these differences could be important in this vulnerable population. For example, the estimated decrease in FEV_1 with an IQR increase in average indoor BC over the previous week [−17.87 mL (95% CI: −33.76, −1.98) for a 0.22-$\mu g/m^3$ increase in integrated filter BC] was consistent with the decrease in FEV_1 associated with an additional 1.5 y of age (−18.26 mL; 95% CI: −37.10, 0.59). These findings are also notable because they were observed at very low average levels of indoor $PM_{2.5}$ (8.61 $\mu g/m^3$) and BC (0.24 $\mu g/m^3$). These levels are 25–50% lower than historic ambient background levels in the United States or the Boston area (Davis et al. 2011; Li et al. 2016; Nyhan et al. 2018). In contrast, there were few consistent associations with ambient exposures. While the patterns were similar, associations with post-bronchodilator pulmonary function tests were weaker than the corresponding associations with pre-bronchodilator measures, suggesting that associations might have been attenuated or masked in participants who used a short-acting bronchodilator prior to clinic visits, since participants did not alter their usual medication use during the study.

Although there is strong evidence of a short-term association between outdoor air pollution and reduced pulmonary function for general population studies in adults, our model estimates did not support effects of ambient BC or $PM_{2.5}$ on pre-bronchodilator function, or of indoor or ambient exposures on post-bronchodilator function (Chen et al. 2017; Huang et al. 2016; Lepeule et al. 2014; Rice et al. 2013; Santos et al. 2016; Thaller et al. 2008; Ulvestad et al. 2015; Wu et al. 2014; Zhao et al. 2015; Zuurbier et al. 2011). Analyses of the association between ambient exposures and pulmonary function in the Framingham Offspring and Third Generation cohorts (Rice et al. 2013) and the Normative Aging Study (Lepeule et al. 2014) were also conducted in the Boston area and utilized daily ambient air pollution data from the same central site monitor. In the Offspring and Third Generation cohorts (n = 3,262, 46% male, on average 52 y old), 1-, 2-, 3-, 5-, and 7-d moving averages of $PM_{2.5}$ prior to spirometry were explored (Rice et al. 2013). Exposures to ambient $PM_{2.5}$ in the previous 1 to 2 days were associated with decreases in FEV_1 and FVC. For the 1 day average before testing, each 5 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with 7.9 (95% CI: −13.5, −2.3)-mL lower FEV_1. This is in contrast to our estimate of −4.1 (95% CI: −17.22, 9.02) mL per 5 $\mu g/m^3$ of ambient $PM_{2.5}$ on lag1. In the Normative Aging Study (n = 776, all males, on average 72 y old), $PM_{2.5}$ and BC lags 4 and 24 h before spirometry and measurements on the 1, 3, 7, 14, and 28 days before were examined on multiple visits. Associations between exposures to BC and $PM_{2.5}$ in the 4 h, 24 h (lag0), or previous day (lag1) before testing and FEV_1 or FVC were null, similar to our findings, although there were associations observed with longer lag periods, i.e., 3- to 28-day moving averages (Lepeule et al. 2014). The reasons for differences between the results in these studies are uncertain, but may have to do with the time spent indoors among our COPD patients and the older participants in the Normative Aging Study, compared to the younger participants in the Framingham study.

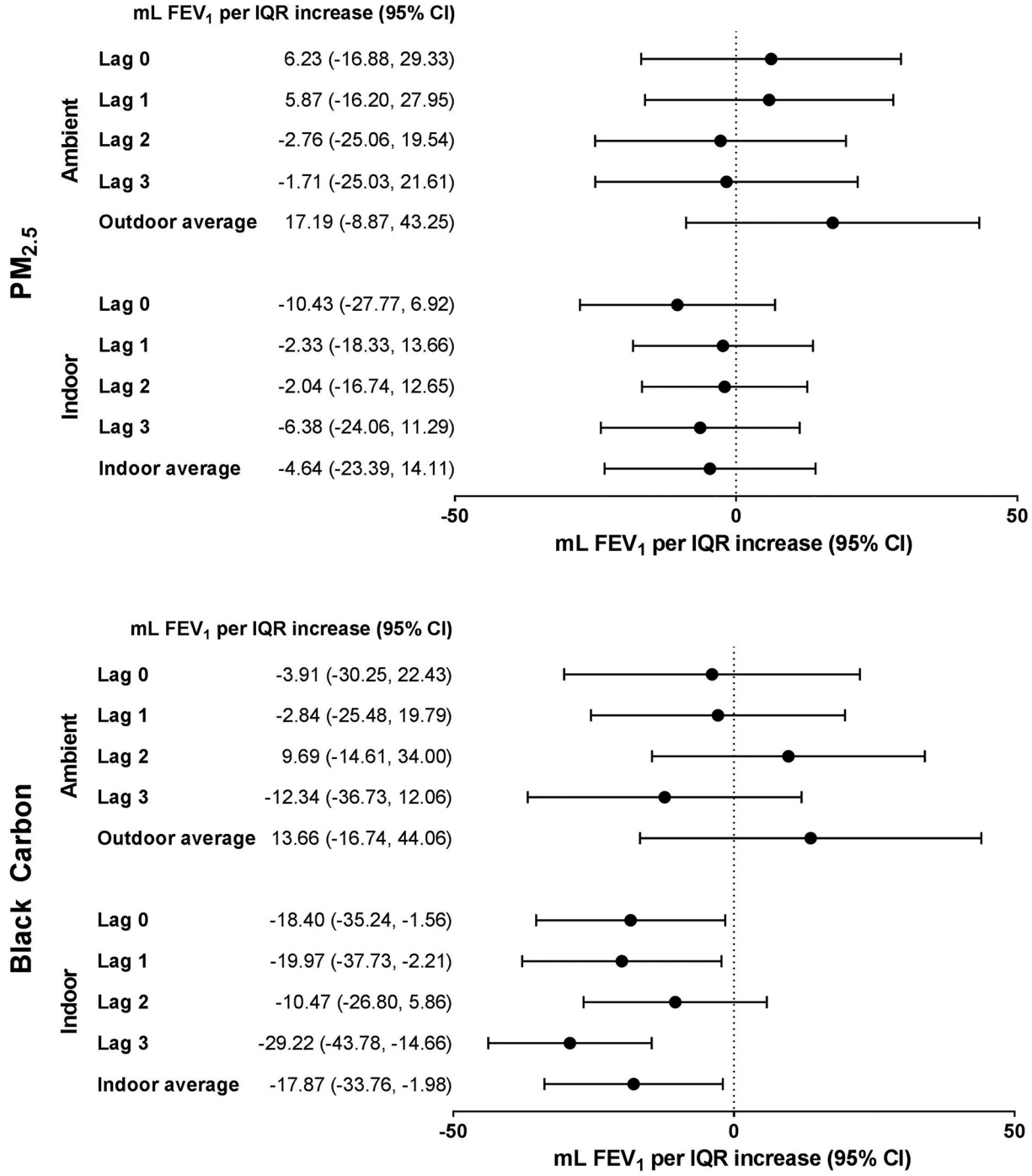

Figure 1. Estimated difference (beta and 95% confidence intervals) in pre-bronchodilator forced expiratory volume in 1 s (FEV_1) (mL) for an interquartile range increase in indoor or ambient particulate matter ≤2.5 μm ($PM_{2.5}$) (top) or black carbon (BC, bottom) among 125 individuals with chronic obstructive pulmonary disease (COPD) living in Eastern Massachusetts, United States (2012–2014). Each exposure is in a separate longitudinal mixed model with a random effect for participant, adjusted for age, gender, race, height, body mass index (BMI), season, ambient temperature and relative humidity on the day of spirometry, pulmonary medication use, self-report of cold or illness in the past 2 weeks, and individual-level socioeconomic status. Interquartile range (IQR) values for each exposure are listed in Table 2.

Previous studies of the impacts of air pollution on lung function in COPD patients have been cross-sectional or have been repeated measures studies with small numbers of participants (<60) (Brauer et al. 2001; de Hartog et al. 2010; Lagorio et al. 2006; Silkoff et al. 2005; Trenga et al. 2006). In a recent meta-analysis, Bloemsma et al. (2016) identified nine studies of ambient PM and FEV_1 in COPD patients. The pooled estimate indicated that each 10-$\mu g/m^3$ increase in PM_{10} (without regard for the specific time window examined) was associated with a 3.38-mL decrease in FEV_1 (95% CI: −6.39, −0.37). In contrast, in this study, each 10-$\mu g/m^3$ increase in indoor $PM_{2.5}$ over the previous week (based on the integrated filter measure) was associated with a 9.2-mL decrease in FEV_1 (95% CI: −41.03, 22.63), and each 10-$\mu g/m^3$ increase in ambient $PM_{2.5}$ over the previous week was associated with a 51.64-mL increase (95% CI: −46.22, 149.50).

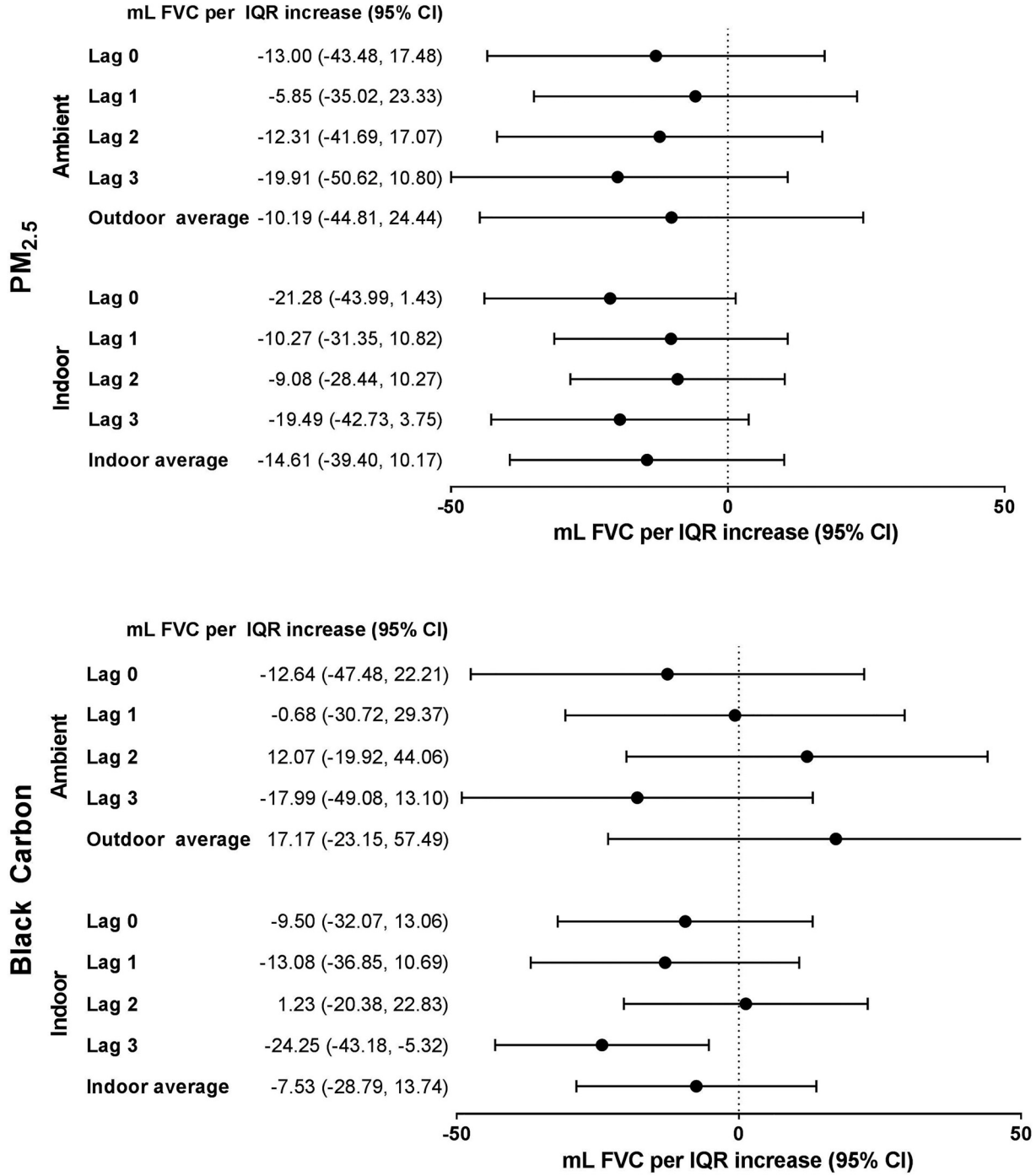

Figure 2. Estimated difference (beta and 95% confidence intervals) in pre-bronchodilator forced vital capacity (FVC) (mL) for an interquartile range increase in indoor or ambient particulate matter ≤2.5 μm ($PM_{2.5}$) (top) or black carbon (BC, bottom) among 125 individuals with chronic obstructive pulmonary disease (COPD) living in Eastern Massachusetts, United States (2012–2014). Each exposure is in a separate longitudinal mixed model with a random effect for participant, adjusted for age, gender, race, height, body mass index (BMI), season, ambient temperature and relative humidity on the day of spirometry, pulmonary medication use, self-report of cold or illness in the past 2 weeks, and individual-level socioeconomic status. Interquartile range (IQR) values for each exposure are listed in Table 2.

Participants in our study were selected to live in homes without major indoor combustion sources, explaining the average and median indoor/outdoor ratios for BC of less than 1. However, the corresponding ratios for $PM_{2.5}$ were above 1, suggesting that there were sources of indoor PM that were unaccounted for. It is also possible that the differences in the ratios could represent differences in the spatial patterns of the pollutants or in the relative importance of the relative height of the central site and in-home samplers. This implies that while our indoor measures of BC are likely mostly a reflection of outdoor exposures that have infiltrated indoors, our indoor measures of $PM_{2.5}$ are likely a mixture of $PM_{2.5}$ of outdoor origin and $PM_{2.5}$ generated indoors.

Our study has a number of limitations. First, we were unable to directly measure daily indoor exposures with our indoor sampler and instead used variability at the central site to estimate variability in daily exposures indoors. This may have induced exposure error,

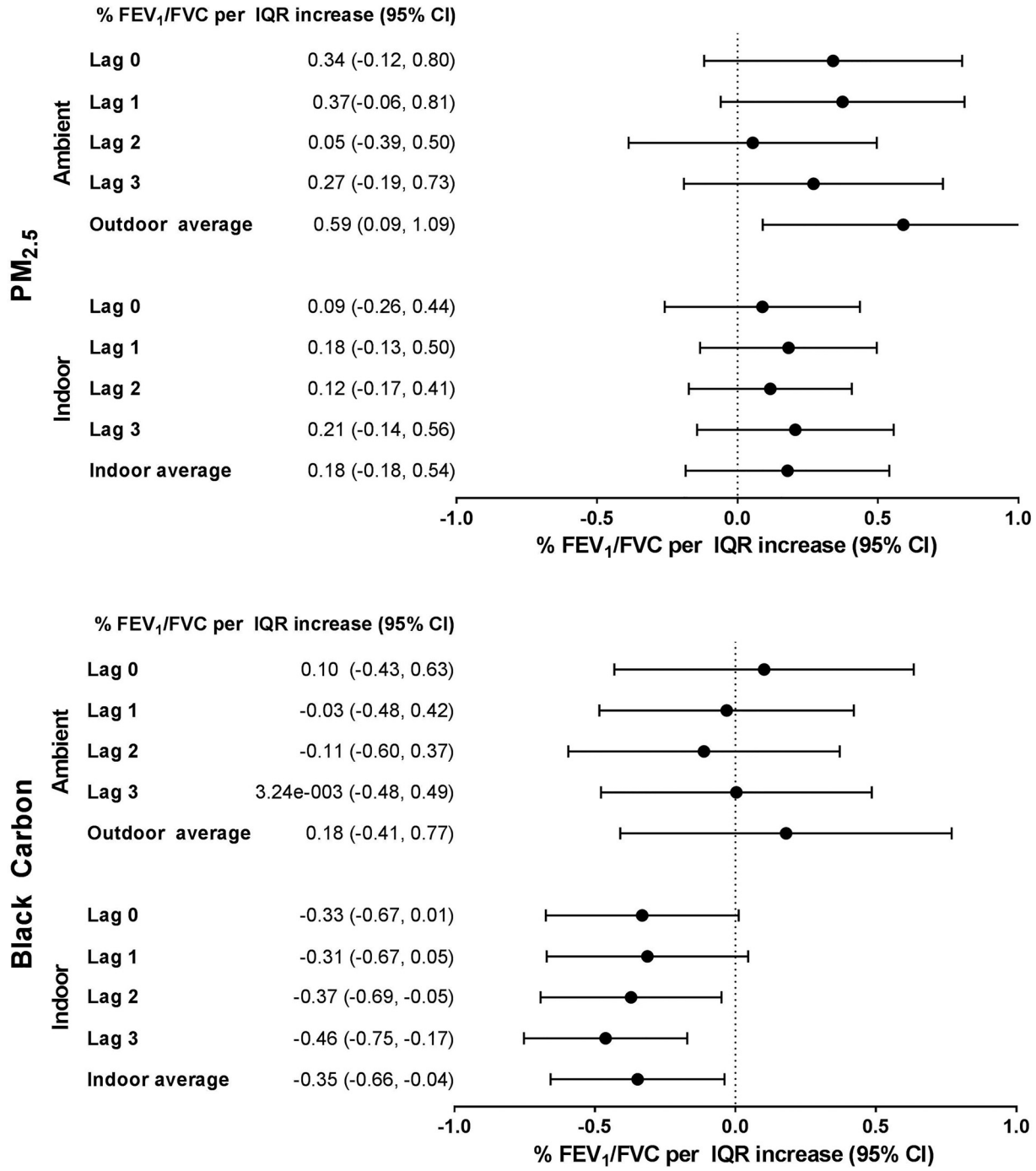

Figure 3. Estimated difference (beta and 95% confidence intervals) in pre-bronchodilator percent forced expiratory volume in 1 s (FEV_1)/FVC for an interquartile range (IQR) increase in indoor or ambient particulate matter ≤2.5 μm ($PM_{2.5}$) (top) or black carbon (BC, bottom) among 125 individuals with chronic obstructive pulmonary disease (COPD) living in Eastern Massachusetts, United States (2012–2014). Each exposure is in a separate longitudinal mixed model with a random effect for participant, adjusted for age, gender, race, BMI, season, ambient temperature and relative humidity on the day of spirometry, pulmonary medication use, self-report of cold or illness in the past 2 weeks, and individual-level socioeconomic status. IQR values for each exposure are listed in Table 2.

although in previous work, we demonstrated a statistically significant relationship between variability in central site concentrations and indoor levels in a subset of these homes (Tang et al. 2018). For both $PM_{2.5}$ and BC, there was little difference in the effect estimates between the individual daily lags and the integrated measures, also suggesting that this was a reasonable approach. Second, the levels of pollution in this study were quite low, limiting our power to detect statistically significant effects. Our results do imply, however, that exposures at these low levels still lead to important decreases in pulmonary function among this vulnerable population. Third, we did not include information on the traffic density outside the home, type of home, or home age as exposures or effect modifiers in our analyses. However, we have shown in previous work that these are determinants of BC indoors among our participants (Tang et al. 2018), suggesting that our measure of indoor BC likely captures the variability in these factors.

Fourth, we did not sample directly outside of the homes of each participant, and therefore, our indoor measures may just be a better estimate of the spatial heterogeneity in these pollutants in Eastern Massachusetts. Lastly, given the demographics of the Boston VA, our study may not be widely generalizable to other populations of parts of the country or to individuals with more severe COPD who may not have been able to participate in our study.

This study also has a number of important strengths. It is one of the largest studies of COPD patients to date, allowing us to balance in-person spirometry by trained staff and in-home measures of exposures along with central site measures of ambient exposures. Unlike many previous studies, we were able to assess the impacts of air pollution on pulmonary function over all seasons, as opposed to only one or two. We were also able to measure indoor exposure for all participants, which, given that our participants spent, on average, 17 h indoors, is likely a reasonable estimate for personal exposures. Lastly, we had extensive information on a number of potential confounders, allowing us to more robustly assess the impacts of indoor and ambient air pollution on pulmonary function.

Conclusions

Among this population of Boston-area individuals with COPD, we observed decreases in pulmonary function measures with increasing indoor air pollution exposures and, in particular, BC. We found less clear evidence of associations between lung function measures and ambient pollution concentrations measured at a central site location. Our findings suggest that individuals with COPD may be a subpopulation susceptible to the health effects of indoor PM and BC. This may suggest that COPD patients could benefit from interventions to reduce their exposure to traffic-related PM in their homes.

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